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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,559	03/07/2002	Yasushi Ochiai	4367-0101P	9100

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,559	OCHIAI ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-7,9,10 and 12-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 10* is/are allowed.

6)☒ Claim(s) *3,5-7,9 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Humera N. Sheikh
HUMERA N. SHEIKH
PATENT EXAMINER
TC-1600

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Applicant's Amendment and Applicant's Arguments/Remarks, both filed 04/25/06 is acknowledged.

Claims 1, 3, 5-7, 9, 10 and 12-14 are pending in this action. Claims 2, 4, 8 and 11 have been cancelled. Claims 3, 5-7, 9 and 12-14 are rejected. Claims 1 and 10 are allowed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 5-7, 9 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pierre *et al.* (US Pat. No. 5,300,318).

Pierre *et al.* teach granulates of alimentary and/or medicinal active principles intended for feeding or treating ruminants are polished by spraying a solution of one or more active principles, resins and/or sugars onto the said active principles. The polished active principles are then coated with a polymer providing protection in the rumen (see Abstract). It is preferred to employ an aqueous solution of active principle and especially a solution sprayed onto a lysine and/or methionine granulate. The base granulate which is subjected to the polishing operation may be made from lysine hydrochloride crystals (col. 1, lines 55-61). The active principle is generally an amino acid such as methionine, lysine or one of its salts, phenylalanine, histidine, arginine, or tyrosine, a medicament such as a vitamin, antibiotic, or antiparasitic agent, or a protein. The preferred active principle is lysine, in which case a homogeneous granulate is obtained, consisting of a lysine core polished with a lysine film (col. 1, line 66 – col. 2, line 9). The granulate is screened so as to retain a granulate distribution between 200 and 4000 μm (col. 2, lines 15-17).

According to Pierre *et al.*, the coating contains at least one component, which is chosen from basic polymers, copolymers or mixtures. The coating mixture solution is sprayed onto the polished granulate using a fluidized bed or any other spraying apparatus (col. 2, line 61 – col. 3, line 20). The granulate obtained after coating exhibits improved stability (col. 3, lines 30-34). Pierre *et al.* are silent regarding the granular strength.

It is the Examiner's position that Applicants have not demonstrated any unexpected or surprising results, which accrue from the claimed granular strength range, since the prior art

clearly teaches a similar process of granulation whereby drug granules are sprayed with a solution of a water soluble drug on a crystal of said water soluble drug and a further coating with a release control film coating agent is applied to the drug granule. The art also teaches obtaining granules that exhibit improved stability over past formulations. No significant distinction is observed between the instant invention and the prior art, since the prior art initially teaches an effective method for the process of forming coated drug granules, whereby the granules provide for enhanced stability, as similarly desired by the Applicant. Furthermore, one of ordinary skill in the art would be fully capable of determining suitable and effective granular strength ranges through the use of routine or manipulative experimentation, to obtain the best possible results, as these are indeed variable parameters established within the art.

Claims 3, 5-7, 9 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koyama *et al.* (US Pat. No. 5,855,914).

Koyama *et al.* teach granules and methods for producing granules having a core and having an increased granule strength, that are produced by spraying core granules with a dispersion of a low substituted hydroxypropylcellulose (L-HPC), and if necessary, simultaneously applying a dusting powder. The granules having a core thus obtained exhibit increased granule strength and improved disintegrating property. An active ingredient, such as drug can be contained in the dispersion, dusting powder or core granules (see Abstract).

The core granules include, for example, spherical granules, based on non-pareil seeds and the core granules in themselves may be a different active ingredient other than the active ingredient contained in the dispersion or dusting powder. The core granules may be coated with

waxes or polymers to produce the cores. The dispersion may additionally have the active ingredient and other additives other than the L-HPC uniformly dispersed and/or dissolved therein (col. 2, lines 30-45). The active ingredients in the form of granules are listed at column 2, lines 46 – col. 3, line 7 and include, for example, drugs for the central nervous system, respiratory organs, digestive organs, etc.

According to Koyama *et al.*, granulation is carried out, while nucleus granules are sprayed with a dispersion and/or solution of L-HPC and the active ingredient and/or additives, if necessary, and are applied with a dusting agent. The granules obtained have a core with uniform particle size (col. 3, line 57 – col. 3, line 4).

The granules are subjected to further coating to provide for flavor-masking coating, enteric coating, gastric coating or sustained-release coating, etc. and may be coated midway during the production for the purpose of stabilization, when the active ingredient is properly formulated. The granules may be filled into capsules or mixed with other components to produce tablets (col. 4, lines 5-13).

Coating agents include, for example, hydroxypropylmethylcellulose phthalate, hydroxypropylmethylcellulose acetate succinate, ethylcellulose, Tween 80 and the like (col. 4, lines 14-23). The granules having a core as obtained by these methods show increased granule strength and improved disintegration property (col. 4, lines 24-26).

The Examples at columns 4-8 demonstrate the production of uniformly coated granules having cores that were free from granule breakage during the coating process in each instance.

While Koyama *et al.* do not teach the instant granular strength (650-2500 gf/mm^2), the Examiner points out that, generally differences in granular strength will not support the

patentability of subject matter encompassed by the prior art unless there is evidence indicating such granular strength is critical. [W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In the instant case, the Applicant's have not demonstrated any unexpected results in the granular strength range claimed. The prior art explicitly teaches processes for forming granules wherein active ingredients are sprayed onto granule cores and also teaches the further subjection of coating on the granules. Even further, the prior art clearly teaches stabilized granules that exhibit increased granular strength and teaches granule cores that are free from granule breakage during the coating process, which is a similar objective desired by Applicant. Therefore, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 04/25/06 have been fully considered but they are not persuasive.

Applicant argued regarding the 35 U.S.C. 103(a) rejection of claims 1, 3, 5-7, 9, 10 and 12-14 over Pierre *et al.* (US '318) and Koyama et al. (US '914) stating, "Neither cited references discloses the presently claimed process for achieving substantially higher granular strengths with respect to the drugs selected from the group consisting of metformin hydrochloride, ethydronic acid di-sodium, cimetidine, carbocisteine, gabapentin, ciprofloxacin hydrochloride, mexiletine

hydrochloride and vancomycin hydrochloride, as currently recited, in part, by claims 1, 3, 7, 10, 12 and 13. The cited references do not disclose each and every element of the presently claimed invention, even in combination. Furthermore, there is no suggestion or 'blazemark' directing the skilled artisan to the selection of the particular compounds recited in the claims."

Applicant's have been fully considered and were found persuasive with regards to method claims 1 and 10. Accordingly, claims 1 and 10 are allowed.

With regards to product claims 3, 5-7, 9 and 12-14, Applicant's arguments remain unpersuasive. While the presently claimed granular strength (650-2500 gf/mm^2) is not explicitly taught, the Examiner points out that, generally differences in granular strength will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such granular strength is critical. [W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The cited references disclose obtaining improved stability and/or uniform content distribution. Applicant's particles merely require particles that have drug loaded upon them. The prior art discloses such particles. The granular strength claimed by Applicant does not impart a patentable distinction over the particles disclosed by the art. Applicants have not demonstrated that the granules of Pierre et al. or Koyama et al. would not have sufficient or ample strength to be suitable for further coating procedures. The Examiner notes that one skilled in the art through routine or manipulative experimentation can readily determine suitable or effective granulation strengths, as these are variable parameters attainable within the art. The prior art recognizes and teaches stablilized granules and particles that are free from granule breakage during the coating

process (see Koyama et al.). The art is directed to stabilized granules having sufficient granular strength, as also desired by Applicant. Thus, for reasons advanced above, the instant invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claims 1 and 10 are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Patent Examiner

Art Unit 1615

July 10, 2006

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